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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,705	10/31/2008	George J. Christ	967001139	9636

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,705	CHRIST ET AL.	
	Examiner	Art Unit	
	QUANG NGUYEN	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,20,25,29,30,33,35 and 43-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 7, 20, 25, 29-30, 33, 35, 43-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/6/2011 has been entered.

Amended claims 1, 7, 20, 25, 29-30, 33, 35, 43-44 and new claims 45-46 are pending in the present application.

Applicants elected previously the following species: (a) penile smooth muscle; (b) maxi K as the elected potassium channel protein; (c) naked DNA transfer; and (d) erectile dysfunction.

Accordingly, claims 1, 7, 20, 25, 29-30, 33, 35, 43-46 are examined on the merits herein **with the above elected species**.

Claim Objections

Claim 29 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 35. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7, 20, 25, 29-30, 33, 35, 43-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. ***This is a new ground of rejection.***

The claims are drawn to a method of enhancing penile smooth muscle relaxation in a subject or a method of treating erectile dysfunction in a subject using an expression construct comprising hSlo operatively linked to **the SMAA promoter of plasmid SMAA-hSlo**, which plasmid contains a kanamycin-resistant gene and wherein **plasmid SMAA-hSlo is derived from plasmid SMAA-EYFP**.

The application discloses **plasmid SMAA-hSlo and plasmid SMAA-EYFP**, that are encompassed by the definitions for **biological material** set forth in 37 C.F.R. § 1.801. The instant specification teaches simply that **the vector SMAA/EYFP is obtained from John Szucsik**, Medical Center of Cinninnati, USA; and **the EYFP gene was removed and hSlo was inserted in its place to give the plasmid SMAA-hSlo**; and that **the SMAA/EYFP itself was derived from pSMP8** (described in Cogan et al, J. Biol. Chem. 270:11310-21, 1999). **It is noted that the cited Cogan**

article is published in 1995 and not in 1999; and that this article does not disclose the plasmid pSMP8 (Applicants are invited to point out the specific page and/or line numbers). More importantly, the instant specification also failed to describe how SMAA/EYFP plasmid was derived in which manner, shape or form from the plasmid pSMP8. Because it is apparent that these biological materials are essential for practicing the claimed invention, it must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809.

It is unclear whether these biological materials are known and readily available to the public or that the written instructions are sufficient to reproducibly construct this biological material from starting materials known and readily available to the public. Accordingly, availability of such biological materials are deemed necessary to satisfy the enablement provisions of 35 U.S.C. § 112. If this biological material is not obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological material. **In order for a deposit to meet all criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants or assignee must provide assurance of compliance with provisions of 37 C.F.R. §§ 1.801-1.809, in the form of a declaration or applicant's representative must provide a statement.** The content of such a declaration or statement is suggested by the enclosed attachment. Because such deposit will not have been made prior to the effective filing date of the instant application, applicant is required to submit a verified statement from a person in a position to corroborate the fact, which states that the biological material which has been

deposited is the biological material specifically identified in the application as filed (37 C.F.R. § 1.804). Such a statement need not be verified if the person is an agent or attorney registered to practice before the Office. Applicant is also reminded that the specification must contain reference to the deposit, including deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7, 20, 25, 29-30, 33, 35, 43-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. ***This is a new ground of rejection.***

Independent claims 1 and 35 are vague and indefinite in that the metes and bounds of the term "derived from" are unclear. It is unclear the nature and number of steps required to obtain the "plasmid SMAA-hSlo" from the "plasmid SMAA-EYFP". It is uncertain which particular components or sequences from the "plasmid SMAA-EYFP" that the "plasmid SMAA-hSlo" should or should not contain. Clarification is requested because the metes and bounds of the claims as written are not clearly determined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 7, 20, 25, 29-30, 33, 35, 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geliebter et al (US 6,150,338; IDS) in view of Leiden et al (US 6,436,907) and evidenced by Foster et al (J. Biol. Chem. 267:11995-12003, 1992; IDS) and Melman et al (Gene therapy 15:364-370, 2008; IDS). ***This is a new ground of rejection.***

The claims are drawn to a method of enhancing penile smooth muscle relaxation in a subject or a method of treating erectile dysfunction in a subject using any expression construct as long as it comprises hSlo operatively linked to **the SMAA promoter of plasmid SMAA-hSlo**. It is noted that the further limitation "which plasmid contains a kanamycin-resistant gene and wherein **plasmid SMAA-hSlo is derived**

from plasmid SMAA-EYFP" simply describes the plasmid SMAA-hSlo from which the SMAA promoter is obtained for use in an expression construct that is utilized in the methods as claimed.

Geliebter et al teach at least a method for enhancing corporal smooth muscle relaxation resulting in a more easily attained erection in a subject, including a subject having erectile dysfunction resulted from a variety of disorders including neurogenic, arteriogenic and veno-occlusive dysfunctions, said method comprises directly injected into **corporal smooth muscle cells** of said subject with **a DNA encoding a maxi-K potassium channel protein (hslo cDNA)** in various forms, including **a naked DNA expression plasmid vector**, and wherein the expression plasmid vector can contain **smooth muscle specific promoters** and enhancers for expressing the encoded maxi-K potassium channel protein (see at least Summary of the Invention; particularly col. 4, lines 16-24, lines 53-65; col. 5, lines 24-44; col. 6, lines 9-49; examples and issued claims).

Geliebter et al do not teach specifically the use of a smooth muscle alpha actin (SMAA) promoter for expressing the encoded maxi-K potassium channel protein, wherein **the utilized SMAA promoter is the SMAA promoter of plasmid SMAA-hSlo**; even though Geliebter et al disclose that **vectors suitable for the expression of hslo cDNA under the expression control of any smooth muscle specific promoter would be apparent to one skilled in the art and they include pET-3d, pcDNA, pcDNA3, pREP10, pRc/CMV among others**.

At the effective filing date of the present application (11/26/2003), Leiden et al already taught at **least the use of a smooth muscle alpha-actin promoter for expressing a desired gene product into vascular smooth muscle cells in both *in vitro* and *in vivo*** (see at least Brief Summary of the Invention; particularly col. 9, line 49 continues to line 11 of col. 10). Leiden et al further **disclosed explicitly the use of a mouse smooth muscle alpha-actin promoter of Foster et al** (J. Biol. Chem. 267:11995-12003, 1992) (col. 10, lines 5-6). Since the SMAA promoter of the pSMAA-hSlo is **a mouse smooth muscle alpha-actin promoter, without any disclosed particular sequence as evidenced by the teachings of Melman et al** (see at least Fig. 1; page 365, col. 1, second paragraph; page 368, col. 1, last paragraph); at least the mouse smooth muscle alpha-actin promoter of Foster et al would meet this limitation.

Accordingly, it would have been obvious for an ordinary skilled artisan to modify the method taught by Geliebter et al by also selecting a smooth muscle alpha-actin promoter, including the mouse smooth muscle alpha-actin promoter of Foster et al, for expressing hSlo cDNA in corporal smooth muscle cells in light of the above teachings of Leiden et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because a smooth muscle alpha-actin promoter, including the mouse smooth muscle alpha-actin promoter of Foster et al, has been used to express a desired gene product in smooth muscle cells as taught by Leiden et al. Furthermore, please

note that Geliebter et al already taught explicitly that any smooth muscle specific promoter can be used.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Geliebter et al., Leiden et al; coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

The method resulting from the combined teachings of Geliebter et al and Leiden et al is indistinguishable from the methods as claimed as evidenced by the teachings of Foster et al and Melman et al.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicants' arguments related in part to the above new ground of rejection in the Amendment filed on 1/6/2011 (page 6) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

Applicants argue basically that the cited references do not render obvious the presently claimed methods, particularly in view of the advantageous results obtained by the pSMAA-hSlo vector used in both the present application and in the previously discussed publication by Melman et al (2008).

Applicants' arguments are moot since as written **the claims do not require the plasmid SMAA-hSlo being directly introduced into a sufficient number of penile**

smooth muscle cells in a subject or into corporal smooth muscle cells of a subject in need of treatment for erectile dysfunction. Rather, the claims are directed to a method of enhancing penile smooth muscle relaxation in a subject or a method of treating erectile dysfunction in a subject using **any expression construct as long as it comprises hSlo operatively linked to the SMAA promoter of plasmid SMAA-hSlo**. It is noted that the further limitation "which plasmid contains a kanamycin-resistant gene and wherein **plasmid SMAA-hSlo is derived from plasmid SMAA-EYFP" simply describes the plasmid SMAA-hSlo from which the SMAA promoter is obtained for use in the expression construct**. Please refer to a new ground of rejection for the currently amended claims as written.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 7, 20, 25, 29-30, 33, 35, 43-46 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over either claims 1-9 of U.S. Patent No. 6,150,338 or over claims 1-3 of U.S. Patent No. 7,030,096 and in view of Leiden et al (US 6,436,907), and evidenced by Foster et al (J. Biol. Chem. 267:11995-12003, 1992; IDS) and Melman et al (Gene therapy 15:364-370, 2008; IDS). ***This is a new ground of rejection.***

Claims 1-9 of US Patent No. 6,150,338 are drawn to a method for inducing penile erection in a subject comprising the introduction and expression of a DNA sequence encoding a maxi-K potassium channel protein into a sufficient number of penile cells of the subject to induce penile erection in the subject.

Claims 1-3 of US Patent No. 7,030,096 are directed to a method of enhancing relaxation of a penile smooth muscle in a subject having heightened contractility of the penile smooth muscle, comprising the direct introduction and expression of a DNA sequence (in the form of a naked DNA) comprising a promoter sequence, including a smooth muscle specific promoter, operably linked to a sequence encoding maxi-K potassium channel protein into a sufficient number of penile smooth muscle cells of the subject.

The claims of the present application differ from the issued claims of either US Patent No. 6,150,338 or US Patent No. 7,030,096 in reciting specifically using the smooth muscle specific promoter SMAA of plasmid SMAA-hSlo.

However, at the effective filing date of the present application (11/26/2003) Leiden et al already taught at least the use of a smooth muscle alpha-actin promoter for expressing a desired gene product into vascular smooth muscle cells in both *in vitro* and *in vivo* (see at least Brief Summary of the Invention; particularly col. 9, line 49 continues to line 11 of col. 10). Leiden et al further disclosed explicitly the use of a mouse smooth muscle alpha-actin promoter of Foster et al (J. Biol. Chem. 267:11995-12003, 1992) (col. 10, lines 5-6). Since the SMAA promoter of the pSMAA-hSlo is a mouse smooth muscle alpha-actin promoter, without any disclosed particular sequence as evidenced by the teachings of Melman et al (see at least Fig. 1; page 365, col. 1, second paragraph; page 368, col. 1, last paragraph); at least the mouse smooth muscle alpha-actin promoter of Foster et al would meet this limitation.

Accordingly, it would have been obvious for an ordinary skilled artisan to modify the method taught by either US 6,436,907 or US 7,030,096 by also selecting a smooth muscle alpha-actin promoter, including the mouse smooth muscle alpha-actin promoter of Foster et al, for expressing hSlo cDNA in corporal smooth muscle cells in light of the above teachings of Leiden et al.

An ordinary skilled artisan would have been motivated to carry out the above modifications because a smooth muscle alpha-actin promoter, including the mouse smooth muscle alpha-actin promoter of Foster et al, has been used to express a desired gene product in smooth muscle cells as taught by Leiden et al. Moreover, please note that both US 6,436,907 and US 7,030,096 already taught explicitly that any smooth muscle specific promoter can be used.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of either US 6,436,907 or US 7,030,096; Leiden et al; coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

The method resulting from the combined teachings of either US 6,436,907 or US 7,030,096 and Leiden et al is indistinguishable from the methods as claimed as evidenced by the teachings of Foster et al and Melman et al.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1. Levy, J. (US 2006/0269521) disclosed improved plasmid shuttle vectors for gene therapy or DNA vaccines; and the vectors have backbones based on a variety of commercial available vectors, including and not limited to pEYFP-C1, pd2EYFP-N1 (see at lest Summary of the Invention; and paragraph 32).

2. Clontech; pEYFP-C1 vector information, pages 1-3, October 2002.

Conclusions

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system

provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/QUANG NGUYEN/

Primary Examiner, AU 1633